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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts the impaired cAMP signaling exhibited in SE-expressing cells. FIG. 1A is a bar graph that shows PKA activation in different cell types, with or without forskolin stimulation. (FIG. 1A abbreviations: NL, normal donors; RA, rheumatoid arthritis; HZ; homozygous tissue typing lines expressing the RA shared epitope; FSK, forskolin; PKA, protein kinase A.) FIG. 1B shows PKA activation over time in different cells. (FIG 1B. abbreviations: L565, murine L cells transfected with *HLA-DRB1*0401*; L259, murine L cells transfected with *HLA-DRB1*0403*, L300, murine L cells transfected with *HLA-DRB1*0404*, min, minutes.) FIG. 1C is a bar graph that shows relative PKA activation in different cells expressing different HLA DRB1 alleles. (FIG. 1C abbreviations: WT, wild type; *0404, murine L cell transfectants expressing *HLA-DRB1*0404, *0403,* murine L cell transfectants expressing *HLA-DRB1*0403;* Q70D, substitution of residue number 70 from glutamine to aspartic acid; R71K, substitution of residue number 71 from arginine to lysine; R71E, substitution of residue number 71 from arginine to glutamic acid; A74E, substitution of residue number 74 from alanine to glutamic acid; E47A, substitution of residue number 74 from glutamic acid to alanine.)

Figure 2 depicts the experimental results confirming that inducible DNA repair signaling is transduced through a cAMP-dependent pathway. (FIG. 2 abbreviations: 2CA, 2-chloroadenosine; PGE_1 , prostaglandin E1, FSK, forskolin; 8-Br-cAMP, 8-bromo-cyclic AMP; H-89, a chemical inhibitor of protein kinase A; 8-Br-cGMP, 8-bromo-cyclic GMP; SNAP, S-nitroso-N-acetyl-penicillamine.) FIG. 2A is a graph which shows DNA repair in the presence of different concentrations of 2CA. FIG. 2B is a graph which shows DNA repair in the presence of different concentrations of PGE.sub.1. FIG. 2C is a graph which shows DNA repair in the presence of different concentrations of forskolin. FIG. 2D is a graph which shows DNA repair in the presence of different concentrations of 8-Br-cAMP. FIG. 2E is a graph which shows DNA

repair in the presence of different concentrations of enprofylline. FIG. 2F is a graph which shows DNA repair in the presence of different concentrations of H-89. FIG. 2G is a graph which shows DNA repair in the presence of different concentrations of 8-Br-cGMP. FIG. 2H is a bar graph which shows DNA repair in the presence or absence of SNAP.

Figure 3 depicts the experimental results assessing the role of Gs protein-coupled receptors in the inducible DNA repair signaling. FIG. 3A shows DNA repair in HEK293/A.sub.2a transfectants in the presence of different concentrations of 2CA. (FIG 3A abbreviations: HEK293/A2a, human embryonic kidney 293 cells transfected with A2a adenosine receptor; 2CA, 2-chloroadenosine; M, Molar.) FIG. 3B shows DNA repair in HEK293/A.sub.2b transfectants in the presence of different concentrations of 2CA. (FIG 3B abbreviations: HEK293/A2b, human embryonic kidney 293 cells transfected with A2b adenosine receptor; 2CA, 2-chloroadenosine; M, Molar.) FIG. 3C is a bar graph that shows DNA repair in HEK293/A.sub.1 transfectants in the presence of different concentrations of 2CA and cAMP. (FIG. 3C abbreviations: HEK293/A1, human embryonic kidney 293 cells transfected with A1 adenosine receptor; 2CA, 2-chloroadenosine; cAMP, cyclic AMP.)

Figure 4 depicts the experimental results demonstrating that SE-expressing DRB1 alleles have a direct inhibitory effect on cAMP-dependent signaling. FIG. 4A is a graph showing DNA repair over time in two transfected cell lines. (FIG. 4A abbreviations: L514, L cells transfected with *HLA-DRB1*0402*; L565, L cells transfected with *HLA-DRB1*0401*.) FIG. 4B is a bar graph which shows DNA repair in different L cell transfectants. (FIG. 1B abbreviations: L565, L cells transfected with *HLA-DRB1*0401*; L514, L cells transfected with *HLA-DRB1*0402*; L259, L cells transfected with *HLA-DRB1*0403*.)

Figure 5 is a bar graph which depicts the experimental results demonstrating that SE-containing peptides inhibit cAMP-mediated DNA repair. (FIG. 5 abbreviations: 65-79*0401, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele; 65-79*0402, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele; 65-79*0403, synthetic peptide corresponding to

amino acids 65-79 of the β chain encoded by the *HLA-DRB*0403* allele; 65-79*0404, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0404* allele.)

Figure 6 is a bar graph which depicts the experimental results demonstrating the inhibition of cAMP-mediated inducible DNA repair by SE-containing peptide-conjugated beads. (FIG. 6 abbreviations: Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; Beads, unconjugated Sepharose beads; Bead*0402, peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele) chemically conjugated to Sepharose beads; ON, overnight; h, hours; min, minutes.)

Figure 7 is an alignment which depicts SE homologies in several proteins. (FIG. 7 abbreviations: H. Laminin, human laminin; M. laminin, mouse laminin; APLP1, amyloid precursor protein-like protein 1; ApoE, apolipoprotein E.)

Figure 8 is a bar graph which depicts the inhibition of cAMP-dependent DNA repair by SE-containing, non DR.beta. proteins. (FIG. 8 abbreviations: H. Laminin, human laminin; M. laminin, mouse laminin; H. Fibronectin, human fibronectin.)

Figure 9 is a bar graph which depicts the results of experiments carried out to determine the SE motif.

Figure 10 presents a characterization of SE-triggered intracellular signaling. FIG. 10A shows cAMP levels in the presence of different concentrations of 2CA and after preincubation with different peptide-conjugated beads. (FIG. 10A abbreviations: 2CA, 2-chloroadenosine; Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; Bead*0402, peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele) chemically conjugated to Sepharose beads; min, minutes; cAMP, cyclic AMP.) FIG. 10B

shows PKA activity following preincubation with different peptide-conjugated beads. (FIG. 10B abbreviations: Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; Bead*0402, peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele) chemically conjugated to Sepharose beads; PKA, protein kinase A; min, minutes.) FIG. 10C shows NO levels following preincubation with different peptide-conjugated beads. (FIG. 10C. abbreviations: NO, nitric oxide; Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; Bead*0402, peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele) chemically conjugated to Sepharose beads; min, minutes.) FIG. 10D shows cGMP levels following exposure to different soluble peptides. (FIG. 10D abbreviations: *0401, soluble peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) *0402, soluble peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele); cGMP, cyclic GMP; min, minutes.) FIG. 10E is a bar graph that shows DNA repair in cells exposed or not to L-NMA and different peptide-conjugated beads. (FIG. 10E abbreviations: Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; Bead*0402, peptide 65-79*0402 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele) chemically conjugated to Sepharose beads; L-NMA, N^G-monomethyl-L-arginine.) FIG. 10F is a bar graph that shows DNA repair in cells preincubated or not with KT5823 and preincubated with different peptide-conjugated beads. (FIG. 10F abbreviations: Bead*0401, peptide 65-79*0401 (corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele) chemically conjugated to Sepharose beads; KT5823, a chemical inhibitor of protein kinase G.)

Figure 11 shows the inhibition of cAMP signaling by SE genetically inserted into foreign proteins. FIG. 11A shows the amino acid sequence of the recombinant HBc proteins containing residues 65-79 of DR.beta.*0401 and DR.beta.*0402. (FIG. 11A abbreviations: HBc*0401, a recombinant chimeric protein, consisted of hepatitis B core protein (HBc) with an insertion of a

sequence corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele; HBc*0402, a recombinant chimeric protein, consisted of hepatitis B core protein (HBc) with an insertion of a sequence corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele.) FIG. 11B is a bar graph which shows DNA repair in M1 cells preincubated overnight with HBc*0401 or HBc*0404. (FIG. 11B abbreviations: HBc*0402, a recombinant chimeric protein, consisted of hepatitis B core protein (HBc) with an insertion of a sequence corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele; HBc*0401, a recombinant chimeric protein, consisted of hepatitis B core protein (HBc) with an insertion of a sequence corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele.)

Figure 12 depicts the neuroprotective effect of SE-containing peptides. (FIG. 12 abbreviations: 65-78*0401, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0401* allele; 65-78*0402, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0402* allele.) FIG. 12A depicts NG108-15 cells after 24 hours of incubation with peptide 65-78*0402. FIG. 12B depicts NG108-15 cells after 24 hours of incubation with peptide 65-78*0401. FIG. 12C is a bar graph that shows cell number and neurites in NG108-15 cells following exposure to different peptides.

Figures 13A-D presents data showing that SE-containing peptides bind to and transduce signaling through the cell surface receptor: calreticulin. FIG. 13A shows immunoblots of recombinant human calreticulin and HSP60 (eluted from peptide affinity chromatography). (FIG. 13A abbreviations: 65-78*0404, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0404* allele; 65-78*0402, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0402* allele; CRT, calreticulin; Hsp60, human 65 kD heat shock protein.) FIG. 13B shows surface plasmon resonance profiles. (FIG. 13B abbreviations: 65-79*0401, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0401* allele; 65-79*0402, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-DRB*0402* allele; 65-79*0404, synthetic peptide corresponding to amino acids 65-79 of the β chain encoded by the *HLA-*

*DRB*0404* allele; RU, response units; s, seconds.) FIG. 13C shows that calreticulin anti-sense oligonucleotides suppress calreticulin surface expression. (FIG. 13C abbreviations: Crt, calreticulin; Crt Anti-sense, cells transfected with Crt anti-sense oligonucleotides; Crt Sense, cells transfected with Crt sense oligonucleotides.) FIG. 13D shows that anti-calreticulin antibodies and anti-sense oligonucleotides block the cAMP-inhibitory effect of SE-containing peptides. (FIG. 13D abbreviations: 65-78*0401, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0401* allele; 65-78*0402, synthetic peptide corresponding to amino acids 65-78 of the β chain encoded by the *HLA-DRB*0402* allele; Crt, calreticulin; Ab, antibody; crkII, control antibody; Crt Antisense Oligo, cells transfected with Crt anti-sense oligonucleotides; Crt Sense Oligo, cells transfected with Crt sense oligonucleotides.)

Figure 14 ([SEQ ID NO: 29]) projects the amino acid sequence of the recombinantly produced calreticulin referenced in the instant application.